DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
DONNA VELASQUEZ
5210 PACIFIC CONCOURSE DRIVE
LOS ANGELES CA 90045

February 25, 2015

Re: K143636
Trade/Device Name: IMMULITE® 2000 Androstenedione Calibration Verification Material, IMMULITE® 2000 Troponin I Calibration Verification Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: I, Reserved
Product Code: JJX
Dated: December 19, 2014
Received: December 22, 2014

Dear Ms. Donna Velasquez:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -A

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143636

Device Name
IMMULITE® 2000 Androstenedione Calibration Verification Material

Indications for Use *(Describe)*
IMMULITE® 2000 Androstenedione Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Androstenedione assay on the IMMULITE 2000 systems

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

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"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143636

Device Name
IMMULITE® 2000 Troponin I Calibration Verification Material

Indications for Use *(Describe)*
IMMULITE® 2000 Troponin I Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Troponin I assay on the IMMULITE 2000 systems

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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SIEMENS

510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: K143636

1. **Submitter**

Mailing Address:	Siemens Healthcare Diagnostics Inc. 5210 Pacific Concourse Drive Los Angeles, CA 90045
Contact Person:	Donna Velasquez Regulatory Technical Specialist
Phone Number:	(310)-645-8200 x7403
Fax Number:	(310)-645-9999
E-mail Address:	donna.velasquez@siemens.com
Date Prepared:	January 22, 2015

2. **Device Name**

Proprietary Name:	IMMULITE® 2000 Androstenedione Calibration Verification Material
Measurand:	Quality Control materials for IMMULITE® 2000 Androstenedione assay
Type of Test:	Calibration Verification Material (CVM) for IMMULITE® 2000 Androstenedione assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)

3. **Predicate Device Name**

	IMMULITE® 2000 Cortisol Calibration Verification Material (CVM)
Predicate 510(k) No:	K141444

4. **Device Description:**

The IMMULITE® 2000 Androstenedione Calibration Verification Material (CVM) contains one set of four vials each 2mL in liquid form. CVM1 contains processed human serum with preservatives. CVM2, CVM3 and CVM4 contain androstenedione in processed human serum matrix with preservative.

5. **Intended Use:**

Indication for Use:	See Indications for Use Statement below The IMMULITE® 2000 Androstenedione Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Androstenedione assay on the IMMULITE 2000 systems
Special Conditions for Use Statement(s):	For prescription use only

Special Instrument Requirements: IMMULITE® 2000 Systems

6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:

A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 Androstenedione Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 Androstenedione CVM	**Predicate Device IMMULITE 2000 Cortisol CVM**
Intended Use	The IMMULITE® 2000 Androstenedione Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Androstenedione assay on the IMMULITE 2000 systems.	The IMMULITE® Cortisol Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Cortisol assay on the IMMULITE 2000 systems
Storage	1-20°C	Same
Form	Liquid	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Matrix	Human Serum with preservatives	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 Androstenedione CVM	**Predicate Device IMMULITE 2000 Cortisol CVM**
Analyte	Androstenedione	Cortisol

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance Specifications for its intend use. The following tests were performed on the candidate device.

Stability Summary**:**

The stability study was conducted to validate real-time shelf life and open component (in-use or open vial) claim for the IMMULITE 2000 Androstenedione Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM. The Calibration Verification Materials are stable up to 3 years when stored at -20°C prior to opening.

Open Component stability studies presents results that support 8 hours of stability at ambient or room temperature (15-25°C).

Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability calibrators/CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2,** and the dose value is determined from the reference calibrator curve.

Table 2: Stability Protocol Summary - LAOCVM Lot 006

CVM Level	Time-Points (Months)			
LAOCVM1	Day 0	15	27	38
LAOCVM2	Day 0	15	27	38
LAOCVM3	Day 0	15	27	38
LAOCVM4	Day 0	15	27	38

For Open Component testing, the results were determined from a 2-point adjustment. Using IMMULITE 2000 Androstenedione (L2KAO) kit lot 336, CVM lot 006 was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions.

Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Androstenedione Calibration Verification Material (CVM) real time and open component stability testing is applied to dose compared to dose at time point zero. The result is required to fall between ±10% for CVM level 2 and 3 and ±13% for CVM level 4 as shown in **Table 3.**

Table 3: Acceptance criteria for stability of IMMULITE 2000 Androstenedione CVM Lot 006

CVM Level	Dose at time 0 (ng/mL)	Guideline Criteria % difference to time 0	Acceptable dose range (ng/mL)
LAOCVM1	**0.00**	**N/A**	**≤ 0.3**
LAOCVM2	**1.93**	**±10%**	**1.74 – 2.12**
LAOCVM3	**6.68**	**±10%**	**6.01 – 7.35**
LAOCVM4	**15.4**	**±13%**	**13.4 – 17.4**

Traceability:

The IMMULITE Androstenedione CVMs are traceable to an internal material which has been gravimetrically prepared. The CVMs are manufactured using qualified materials and measurement procedures.

Value Assignment:
The IMMULITE Androstenedione CVMs are 4 level materials which are a subset of 7 level Androstenedione calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Androstenedione reagents and two point adjustors. The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The CVMs are manufactured using qualified materials and measurement procedures. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples, spiked patient samples and controls using the assigned CVM values. Four levels of commercially available controls and 28 samples (10 normal female serum samples and 18 spiked samples) were used to validate calibrator/CVM value assignments.

Expected Values/Target Values/Reference Range:
Each CVM level was tested for a total of 27 replicates; 9 runs and 3 replicates per run, 3 different reagent kit lots and 8 IMMULITE 2000 systems. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The target values are provided in the IMMULITE® 2000 CVM Calibration verification Material lot-specific value card. The expected assay range is 0.3 to 10 ng/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Analyte Target Range Values

Analyte target levels	**CVM Level**	**Target Mean (ng/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (ng/mL)**	
	LAOCVM1	0.00	-	0.00	≤0.30
	LAOCVM2	1.31	0.10	1.11	1.51
	LAOCVM3	5.00	0.25	4.50	5.50
	LAOCVM4	10.0	0.65	8.70	11.3
Assay Range	0.3 to10 ng/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 Androstenedione Calibration Verification Material is substantially equivalent to the predicate device intended for similar use. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 Androstenedione Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

SIEMENS

510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: K143636

1. **Submitter**

Mailing Address:	Siemens Healthcare Diagnostics Inc. 5210 Pacific Concourse Drive Los Angeles, CA 90045
Contact Person:	Donna Velasquez Regulatory Technical Specialist
Phone Number:	(310) 645-8200 x7403
Fax Number:	(310) 645-9999
E-mail Address:	donna.velasquez@siemens.com
Date Prepared:	January 22, 2015

2. **Device Name**

Proprietary Name:	IMMULITE® 2000 Troponin I Calibration Verification Material
Measurand:	Quality Control materials for IMMULITE® 2000 Troponin I assay
Type of Test:	Calibration Verification Material (CVM) for IMMULITE® 2000 Troponin I assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)

3. **Predicate Device Name**	IMMULITE 2000 Prolactin Calibration Verification Material (CVM)
Predicate 510(k) No:	K140818
4. **Device Description:**	The IMMULITE® 2000 Troponin I Calibration Verification Material (CVM) contains one set of four vials, 2mL each after reconstitution. CVM1 contains equine serum with 0.88% sodium azide and preservative. CVM2, CVM3 and CVM4 contain human Troponin I and rabbit Troponin C in equine serum matrix with 0.88% sodium azide and preservative.
5. **Intended Use:** **Indication for Use:**	See Indications for Use Statement below The IMMULITE® 2000 Troponin I Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Troponin I assay on the IMMULITE 2000 systems
Special Conditions for Use Statement(s):	For prescription use only

Special Instrument Requirements: IMMULITE® 2000 Systems

6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:

A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 Troponin I Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 Troponin I CVM	**Predicate Device IMMULITE 2000 Prolactin CVM**
Intended Use	The IMMULITE® 2000 Troponin I Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Troponin I assay on the IMMULITE 2000 systems	The IMMULITE® Prolactin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Prolactin assay on the IMMULITE 2000 systems
Form	Lyophilized	Same
Matrix	Equine serum with preservatives	Same
Levels	4	Same
Stability	Stable unopened until the expiration date	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 Troponin I CVM	**Predicate Device IMMULITE 2000 Prolactin CVM**
Storage	≤-20°C	2-8°C
Analyte	Troponin I	Prolactin

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intend use. The following tests were performed on the candidate device.

Stability Summary**:**

The stability study was conducted to validate real-time shelf life and open component (in-use or open vial) claim for the IMMULITE 2000 Troponin I Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM. The Calibration Verification Materials are stable up to 10 months when stored at -20°C prior to opening, and for 2 hours at ambient or room temperature (15-25°C) after reconstitution.

Stability Protocol Summary:
The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

Table 2: Stability Protocol Summary – LTICVM Lot 010

CVM Level	Time-Points (Months)			
LTICVM1	Day 0	3	9	10
LTICVM2	Day 0	3	9	10
LTICVM3	Day 0	3	9	10
LTICVM4	Day 0	3	9	10

For Open Component testing, the results were determined from a 2-point adjustment. Using IMMULITE 2000 Troponin I (L2KTI2) kit lot 270, CVM lot 090 was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions.

Stability Acceptance Criteria Summary:
The Acceptance Criteria for the IMMULITE 2000 Troponin I CVM for real time stability and Open-Component testing is applied to dose compared to dose at time point zero. The result is required to fall between ±10% difference for CVM levels 2, 3 and 4 as shown in **Table 3**.

Table 3: Acceptance criteria for stability of IMMULITE 2000 Troponin I CVM Lot 010

CVM level	**Dose at Time 0 (ng/mL)**	**Guideline Criteria % difference to Time 0**	**Acceptable dose range (ng/mL)**
LTICVM1	**0.00**	**N/A**	**≤0.20**
LTICVM2	**0.56**	**±10%**	**0.50 – 0.62**
LTICVM3	**13.8**	**±10%**	**12.4 – 15.2**
LTICVM4	**159**	**±10%**	**143 - 175**

Traceability:
The IMMULITE Troponin I CVMs are traceable to an internal standard which has been gravimetrically prepared. The CVMs are manufactured using qualified materials and measurement procedures.

Value Assignment:
The IMMULITE Troponin I CVMs are 4 level materials which are a subset of 10 level Troponin I calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Troponin I reagents and two point adjustors. The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. The CVM values are then averaged

across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The controls must fall within their target ranges. Three levels of commercially available controls and 25 spiked samples were used to validate calibrator/CVM value assignments.

Expected Values/Target Values/Reference Range:
The CVMs are manufactured using qualified materials and measurement procedures. The Troponin I CVMs were tested on 15 replicates in total comprised of 5 runs and 3 replicates per run on 4 IMMULITE 2000 systems and 2 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. The CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected assay range is up to 180 ng/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Analyte Target Range Levels

Analyte target levels	**CVM Level**	**Target Mean (ng/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (ng/mL)**	
	LTICVM1	0.00	-	0.00	≤0.20
	LTICVM2	0.575	0.092	0.391	0.759
	LTICVM3	14.2	0.90	12.4	16.0
	LTICVM4	159	15.0	129	189
Assay Range	Up to 180 ng/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 Troponin I Calibration Verification Material is substantially equivalent to the predicate device intended for similar use. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 Troponin I Calibration Verification Material does not

raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.